Remarks

Claims 1, 9-10, and 18 are currently presented.

A replacement sequence listing, including the primers, is enclosed. The specification is also amended accordingly. No new matter is introduced by these amendments.

Claims 1, 9-10, and 18 stand rejected under 35 USC §112, first paragraph, as lacking an adequate written description. The office action states that there appears to be no written description in the specification that fragments of the full-length toxin of SEQ ID NO:8 are insecticidally active; thus polynucleotides encoding insecticidally active fragments of SEQ ID NO:8 are also lacking in the written description. The applicants respectfully traverse this rejection.

The specification describes the use of pesticidal proteins in proforms, as well as non-proform versions, *i.e.*, a pesticidal core toxin fragment of SEQ ID NO:8. Page 11, lines 1-3, of the specification states, "Where the pesticide is in a proform, the method of inactivation should be selected so as not to inhibit processing of the proform to the mature form of the pesticide by the target pest pathogen [emphasis added]." The method of inactivation refers to inactivating cells that produce the polypeptide pesticide. Stating "where" a proform is used clearly means that non-proforms were also contemplated. This quote also shows that more than one proform (*i.e.*, a protoxin having some protoxin portion, but not the full-length protoxin) was contemplated, and that such embodiments were also included in the scope of the invention.

Höfte *et al.* (1989), which is a review of *B.t.* toxins, explains protoxins and core toxins in more detail. A copy is enclosed. For example, the second paragraph of Höfte explains that most crystal proteins are protoxins that are protealytically converted into smaller toxic polypeptides in the insect midgut. The "*cry*I Genes" section of Höfte (SEQ ID NO:8 is a *Cry*1F protein) further explains that *Cry*1 proteins were the best-studied crystal proteins. Their full-length form, of about 130-140 kDa, is proteolytically converted into a toxic core fragment of 60-70 kDa. After explaining this, Höfte states, "This activation can also be carried out *in vitro* with a variety of proteases. The toxic domain is localized in the N-terminal half of the protoxin."

Thus, proform and non-proform toxins were included within the scope of the subject invention, and this was stated (and described) in the specification. The above quote from

page 11 of the specification also illustrates that directly administering truncated toxins to the target pests was described and possessed. The specification describes administering cells directly to pests wherein the cells were transformed to express and harbor proform or non-proform toxins. The specification discusses feeding (or providing) such cells to the target pest. These cells were produced by making and using plasmids and/or vectors comprising polynucleotides encoding proform or non-proform pesticidal proteins. As an alternative to administering treated bacterial cells, Example 3 of the specification states that recombinant plants (comprising individual cells) could be regenerated from plant cells transfected with plasmids and/or vectors of the subject invention.

The above also illustrates that the subject invention also includes polynucleotides that encode pesticidal proteins of the subject invention in any of their various forms. Further support can be found in the Brief Summary, for example, which states, "Also disclosed and claimed are novel toxin genes which express toxins toxic to lepidopteran insects. These toxin genes can be transferred to suitable hosts via a plasmid vector." Originally filed claim 27 of USSN 07/451,261 was directed to "A recombinant DNA transfer vector comprising DNA having all or part of the nucleotide sequence which codes for an amino acid sequence selected from the group consisting of the sequence shown in Table 2, Table 5, Table 8, and Table 11 [emphasis added]." Again, DNA molecules encoding pesticidal proteins were clearly described as being part of the subject invention.

There are several other passages in the specification that further indicate that known modifications could be made to the exemplified, full-length toxins and genes, and that such modifications were considered to be within the scope of the subject invention. For example, the last sentence of Example 4 states, "Thus, the subject invention includes mutants of the amino acid sequence depicted herein which do not alter the protein secondary structure, or if the structure is altered, the biological activity is retained to some degree."

In light of all the foregoing, the applicants respectfully submit that insecticidal fragments of SEQ ID NO:8, and polynucleotides that encode such fragments, were described in the specification as filed. Thus, the withdrawal of this written description rejection is respectfully requested.

Claims 1, 9-10, and 18 stand rejected under 35 USC §112, first paragraph, as lacking enablement. As alleged in the office action, what is not described cannot be enabled. The applicants respectfully traverse this rejection.

As discussed above, pesticidal fragments of SEQ ID NO:8 and polynucleotides that encode them were clearly intended to be part of the subject invention, and they were described as such in the specification. Techniques for making and using such proteins and polynucleotides were also discussed in the specification and were known in the art. For example, page 18 of the specification states that various cloning procedures were conducted using standard procedures, such as those of Maniatis (1982), including genetic engineering techniques to extract DNA from microbial cells, perform restriction enzyme digestion, electrophorese DNA fragments, tail and anneal plasmid and insert DNA, ligate DNA, transform cells, prepare plasmid DNA, electrophorese proteins, and sequence DNA. The specification also states that plasmids containing the *B.t.* toxin genes can be removed from the transformed host microbes by use of standard well-known procedures.

As discussed above, plasmids and/or vectors constructed using these techniques could them be introduced into cells so that the cells produce proform and/or non-proform toxins. Such cells could be later treated to preserve the pesticidal protein. Alternatively, recombinant plants (producing pesticidal proteins) could be regenerated from plant cells transfected using such vectors and the techniques described in Example 3, for example.

In light of all the foregoing, it should be clear that the specification taught the skilled artisan how to make and use the full scope of what is claimed. Thus, the withdrawal of this rejection for lack of enablement is respectfully requested.

Claims 1, 9-10, and 18 stand rejected for obviousness-type double patenting in light of all the claims of U.S. Patent No. 5,188,960. Thus, the office action indicates that what is now claimed (polynucleotides encoding pesticidal fragments of SEQ ID NO:8) is obvious in light of, for example, an isolated DNA encoding a *B.t.* toxin encoding the amino acid sequence of SEQ ID NO:8, and DNA having a nucleotide sequence shown in SEQ ID NO:7. A terminal disclaimer is attached. In light of this, the withdrawal of this rejection for obviousness-type double patenting is respectfully requested.

The applicants believe that this application is in condition for allowance, and such action is earnestly solicited.

The Assistant Commissioner is hereby authorized to charge any fees under 37 CFR §§1.16 and 1.17 as required by this paper to Deposit Account 19-0065.

The applicants invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,

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JMS/ehm
Attachments: Substitute Sequence Listing on paper (32 pages)
Substitute Sequence Listing in Computer Readable Format (disk)
Statement regarding Substitute Sequence Listing
Höfte *et al.* (1989) reference
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